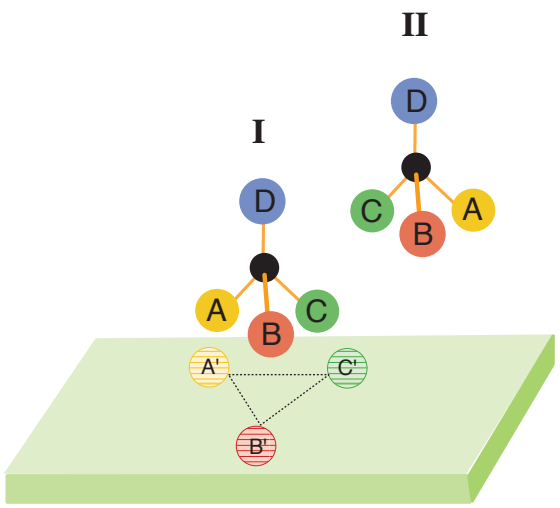
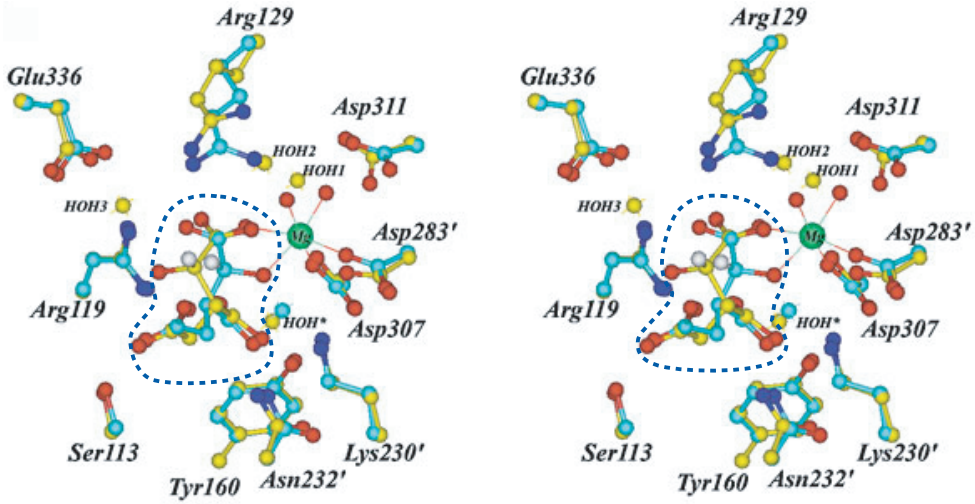
Decades-Old Theory of Enzyme Selectivity Challenged

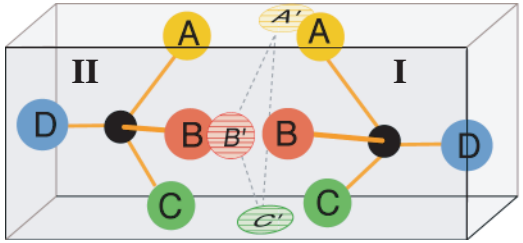
"Three Point Landing" May Not Be Sufficient to Distinguish Optical Isomers



Classical "three point attachment" model of substrate molecule binding to an enzyme surface in preparation for its conversion to product. Atom groups A, B, C (I) of substrate bind their complementary sites A', B', C' on the enzyme surface, exposing D for reaction. The atoms in optical isomer II, the mirror image of I, cannot “match up” to the sites on the enzyme and thus, cannot bind.



3-D reconstruction of structure of binding site of enzyme, with both substrates (L-isocitrate, yellow with red; or D-isocitrate, blue with red) circled, and binding at the center.The D-isomer binds only if Mg^{++} is present, the L-isomer if it is not. Allowing the two images to fuse, by crossing the viewer's eyes, provides a 3-D image of the structure.



Without directional constraint on position of D, either isomer can bind to enzyme surface, here the inside surface of the rectangular solid.

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